

WHAT IS CLAIMED IS:

1. A purified or isolated nucleic acid sequence comprising a nucleotide sequence consisting essentially of one of SEQ ID NOs: 8-3795, wherein expression of said nucleic acid inhibits proliferation of a cell.

5 2. A purified or isolated nucleic acid comprising a fragment of one of SEQ ID NOs.: 8-3795, said fragment selected from the group consisting of fragments comprising at least 10, at least 20, at least 25, at least 30, at least 50 and more than 50 consecutive nucleotides of one of SEQ ID NOs: 8-3795.

10 3. A purified or isolated antisense nucleic acid comprising a nucleotide sequence complementary to at least a portion of an intragenic sequence, intergenic sequence, sequences spanning at least a portion of two or more genes, 5' noncoding region, or 3' noncoding region within an operon comprising a proliferation-required gene whose activity or expression is inhibited by an antisense nucleic acid comprising the nucleotide sequence of one of SEQ ID NOs.: 8-3795.

15 4. A purified or isolated nucleic acid comprising a nucleotide sequence having at least 70% identity to a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 8-3795, fragments comprising at least 25 consecutive nucleotides of SEQ ID NOs.: 8-3795, the nucleotide sequences complementary to SEQ ID NOs.: 8-3795 and the sequences complementary to fragments comprising at least 25 consecutive
20 nucleotides of SEQ ID NOs.: 8-3795 as determined using BLASTN version 2.0 with the default parameters.

25 5. A vector comprising a promoter operably linked to a nucleic acid encoding a polypeptide whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence of any one of SEQ ID NOs.: 8-3795.

30 6. A purified or isolated polypeptide comprising a polypeptide whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence of any one of SEQ ID NOs.: 8-3795, or a fragment selected from the group consisting of fragments comprising at least 5, at least 10, at least 20, at least 30, at least 40, at least 50, at least 60 or more than 60 consecutive amino acids of one of the said polypeptides.

7. A purified or isolated polypeptide comprising a polypeptide having at least 25% amino acid identity to a polypeptide whose expression is inhibited by a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID

NOs.: 8-3795, or at least 25% amino acid identity to a fragment comprising at least 10, at least 20, at least 30, at least 40, at least 50, at least 60 or more than 60 consecutive amino acids of a polypeptide whose expression is inhibited by a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 8-3795 as determined using FASTA version 3.0t78 with the default parameters.

8. A method of producing a polypeptide, comprising introducing a vector comprising a promoter operably linked to a nucleic acid comprising a nucleotide sequence encoding a polypeptide whose expression is inhibited by an antisense nucleic acid comprising one of SEQ ID NOs.: 8-3795 into a cell.

9. A method of inhibiting proliferation of a cell in an individual comprising inhibiting the activity or reducing the amount of a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 8-3795 or inhibiting the activity or reducing the amount of a nucleic acid encoding said gene product.

10. A method for identifying a compound which influences the activity of a gene product required for proliferation, said gene product comprising a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 8-3795, said method comprising:

contacting said gene product with a candidate compound; and

determining whether said compound influences the activity of said gene product.

11. A method for identifying a compound or nucleic acid having the ability to reduce the activity or level of a gene product required for proliferation, said gene product comprising a gene product whose activity or expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 8-3795, said method comprising:

(a) contacting a target gene or RNA encoding said gene product with a candidate compound or nucleic acid; and

(b) measuring an activity of said target.

12. A method for identifying a compound which reduces the activity or level of a gene product required for proliferation of a cell, wherein the activity or expression of said gene product is inhibited by an antisense nucleic acid comprising a nucleotide

sequence selected from the group consisting of SEQ ID NOs.: 8-3795, said method comprising the steps of:

(a) providing a sublethal level of an antisense nucleic acid comprising a nucleotide sequence complementary to a nucleic acid comprising a nucleotide sequence encoding said gene product in a cell to reduce the activity or amount of said gene product in said cell, thereby producing a sensitized cell;

(b) contacting said sensitized cell with a compound; and

(c) determining the degree to which said compound inhibits proliferation of said sensitized cell relative to a cell which does not contain said antisense nucleic acid.

13. A method for inhibiting cellular proliferation comprising introducing an effective amount of a compound with activity against a gene whose activity or expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 8-3795 or a compound with activity against the product of said gene into a population of cells expressing said gene.

14. A composition comprising an effective concentration of an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 8-3795, or a proliferation-inhibiting portion thereof in a pharmaceutically acceptable carrier.

15. A method for inhibiting the activity or expression of a gene in an operon required for proliferation wherein the activity or expression of at least one gene in said operon is inhibited by an antisense nucleic acid comprising a sequence selected from the group consisting of SEQ ID NOs.: 8-3795, said method comprising contacting a cell in a cell population with an antisense nucleic acid complementary to at least a portion of said operon.

16. A method for identifying a gene which is required for proliferation of a cell comprising:

(a) contacting a cell with an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 8-3795, wherein said cell is a cell other than the organism from which said nucleic acid was obtained;

(b) determining whether said nucleic acid inhibits proliferation of said cell; and

(c) identifying the gene in said cell which encodes the mRNA which is complementary to said antisense nucleic acid or a portion thereof.

5 17. A method for identifying a compound having the ability to inhibit proliferation of a cell comprising:

(a) identifying a homolog of a gene or gene product whose activity or level is inhibited by a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs. 8-3795 in a test cell, wherein said test cell is not the cell from which said nucleic acid was obtained ;

(b) identifying an inhibitory nucleic acid sequence which inhibits the activity of said homolog in said test cell;

(c) contacting said test cell with a sublethal level of said inhibitory nucleic acid, thus sensitizing said cell;

10 15 (d) contacting the sensitized cell of step (c) with a compound; and

(e) determining the degree to which said compound inhibits proliferation of said sensitized cell relative to a cell which does not contain said inhibitory nucleic acid.

20 18. A method of identifying a compound having the ability to inhibit proliferation comprising:

(a) contacting a test cell with a sublethal level of a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs. 8-3795 or a portion thereof which inhibits the proliferation of the cell from which said nucleic acid was obtained, thus sensitizing said test cell;

25 (b) contacting the sensitized test cell of step (a) with a compound; and

(c) determining the degree to which said compound inhibits proliferation of said sensitized test cell relative to a cell which does not contain said nucleic acid.

30 19. A method for identifying a compound having activity against a biological pathway required for proliferation comprising:

(a) sensitizing a cell by providing a sublethal level of an antisense nucleic acid complementary to a nucleic acid encoding a gene product required

for proliferation, wherein the activity or expression of said gene product is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 8-3795, in said cell to reduce the activity or amount of said gene product;

5

(b) contacting the sensitized cell with a compound; and

(c) determining the degree to which said compound inhibits the growth of said sensitized cell relative to a cell which does not contain said antisense nucleic acid.

10

20. A method for identifying a compound having the ability to inhibit cellular proliferation comprising:

(a) contacting a cell with an agent which reduces the activity or level of a gene product required for proliferation of said cell, wherein said gene product is a gene product whose activity or expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 8-3795;

15

(b) contacting said cell with a compound; and

(c) determining whether said compound reduces proliferation of said contacted cell by acting on said gene product.

20

21. A method for identifying the biological pathway in which a proliferation-required gene or its gene product lies, wherein said gene or gene product comprises a gene or gene product whose activity or expression is inhibited by an antisense nucleic acid comprising a sequence selected from the group consisting of SEQ ID NOs.: 8-3795, said method comprising:

25

(a) providing a sublethal level of an antisense nucleic acid which inhibits the activity of said proliferation-required gene or gene product in a test cell;

(b) contacting said test cell with a compound known to inhibit growth or proliferation of a cell, wherein the biological pathway on which said compound acts is known; and

30

(c) determining the degree to which said proliferation of said test cell is inhibited relative to a cell which was not contacted with said compound.

22. A method for determining the biological pathway on which a test compound acts comprising:

comprising at least 25 consecutive nucleotides of SEQ ID NOs.: 3796-3800, 3806-4860, 5916-10012 as determined using BLASTN version 2.0 with the default parameters.

28. A method of inhibiting proliferation of a cell comprising inhibiting the activity or reducing the amount of a gene product in said cell or inhibiting the activity or reducing the amount of a nucleic acid encoding said gene product in said cell, wherein said gene product is selected from the group consisting of a gene product having having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 8-3795, a gene product encoded by a nucleic acid having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a nucleic acid encoding a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 8-3795, a gene product having at least 25% amino acid identity as determined using FASTA version 3.0t78 with the default parameters to a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 8-3795, a gene product encoded by a nucleic acid which hybridizes to a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 8-3795 under stringent conditions, a gene product encoded by a nucleic acid which hybridizes to a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 8-3795 under moderate conditions, and a gene product whose activity may be complemented by the gene product whose activity is inhibited by a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 8-3795.

29. A method for identifying a compound which influences the activity of a gene product required for proliferation comprising:

contacting a candidate compound with a gene product selected from the group consisting of a gene product having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID

031542-03104
SUB C11

5

10

15

20

25

30

NOs.: 8-3795, a gene product encoded by a nucleic acid having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a nucleic acid encoding a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs: 8-3795, a gene product having at least 25% amino acid identity as determined using FASTA version 3.0t78 with the default parameters to a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 8-3795, a gene product encoded by a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleic acid selected from the group consisting of SEQ ID NOs.: 8-3795 under stringent conditions, a gene product encoded by a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleic acid selected from the group consisting of SEQ ID NOs.: 8-3795 under moderate conditions, and a gene product whose activity may be complemented by the gene product whose activity is inhibited by a nucleic acid selected from the group consisting of SEQ ID NOs: 8-3795; and

determining whether said candidate compound influences the activity of said gene product.

30. A method for identifying a compound or nucleic acid having the ability to reduce the activity or level of a gene product required for proliferation comprising:

(a) providing a target that is a gene or RNA, wherein said target comprises a nucleic acid that encodes a gene product selected from the group consisting of a gene product having having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 8-3795, a gene product encoded by a nucleic acid having at least 70% nucleic acid identity as determined using BLASTN version 2.0 with the default parameters to a nucleic acid encoding a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs: 8-3795, a gene product having at

least 25% amino acid identity as determined using FASTA version 3.0t78 with the default parameters to a gene product whose expression is inhibited by an antisense nucleic acid comprising a sequence selected from the group consisting of SEQ ID NOs.: 8-3795, a gene product encoded by a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleic acid selected from the group consisting of SEQ ID NOs.: 8-3795 under stringent conditions, a gene product encoded by a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleic acid selected from the group consisting of SEQ ID NOs.: 8-3795 under moderate conditions, and a gene product whose activity may be complemented by the gene product whose activity is inhibited by a nucleic acid selected from the group consisting of SEQ ID NOs: 8-3795;

(b) contacting said target with a candidate compound or nucleic acid; and

(c) measuring an activity of said target.

31. A method for identifying a compound which reduces the activity or level of a gene product required for proliferation of a cell comprising:

(a) providing a sublethal level of an antisense nucleic acid

complementary to a nucleic acid encoding said gene product in a cell to reduce the activity or amount of said gene product in said cell, thereby producing a sensitized cell, wherein said gene product is selected from the group consisting of a gene product having having at least 70% nucleic acid identity as determined using BLASTN version 2.0 with the default parameters to a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 8-3795, a gene product encoded by a nucleic acid having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a nucleic acid encoding a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs:8-3795, a gene product having at least 25% amino acid identity as determined using FASTA version 3.0t78 with the default parameters to a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 8-3795, a gene product encoded by a nucleic acid

comprising a nucleotide sequence which hybridizes to a nucleic acid selected from the group consisting of SEQ ID NOs.: 8-3795 under stringent conditions, a gene product encoded by a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 8-3795 under moderate conditions, and a gene product whose activity may be complemented by the gene product whose activity is inhibited by a nucleic acid selected from the group consisting of SEQ ID NOs: 8-3795;

(b) contacting said sensitized cell with a compound; and

(c) determining the degree to which said compound inhibits the growth of said sensitized cell relative to a cell which does not contain said antisense nucleic acid.

32. A method for inhibiting cellular proliferation comprising introducing a compound with activity against a gene product or a compound with activity against a gene encoding said gene product into a population of cells expressing said gene product, wherein said gene product is selected from the group consisting of a gene product having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 8-3795, a gene product encoded by a nucleic acid having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a nucleic acid encoding a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs:8-3795, a gene product having at least 25% amino acid identity as determined using FASTA version 3.0t78 with the default parameters to a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 8-3795, a gene product encoded by a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleic acid selected from the group consisting of SEQ ID NOs.: 8-3795 under stringent conditions, a gene product encoded by a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleic acid selected from the group consisting of SEQ ID NOs.: 8-3795 under moderate conditions, and a gene product

whose activity may be complemented by the gene product whose activity is inhibited by a nucleic acid selected from the group consisting of SEQ ID NOs: 8-3795.

33. A preparation comprising an effective concentration of an antisense nucleic acid in a pharmaceutically acceptable carrier wherein said antisense nucleic acid is selected from the group consisting of a nucleic acid comprising a sequence having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 8-3795 or a proliferation-inhibiting portion thereof, a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleic acid selected from the group consisting of SEQ ID NOs.: 8-3795 under stringent conditions, and a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleic acid selected from the group consisting of SEQ ID NOs.: 8-3795 under moderate conditions.

34. A method for inhibiting the activity or expression of a gene in an operon which encodes a gene product required for proliferation comprising contacting a cell in a cell population with an antisense nucleic acid comprising at least a proliferation-inhibiting portion of said operon in an antisense orientation, wherein said gene product is selected from the group consisting of a gene product having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 8-3795, a gene product encoded by a nucleic acid having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a nucleic acid encoding a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs:8-3795, a gene product having at least 25% amino acid identity as determined using FASTA version 3.0t78 with the default parameters to a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 8-3795, a gene product encoded by a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleic acid selected from the group consisting of SEQ ID NOs.: 8-3795 under stringent conditions, a gene product encoded by a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleic acid selected from the group consisting of SEQ ID NOs.:

8-3795 under moderate conditions, and a gene product whose activity may be complemented by the gene product whose activity is inhibited by a nucleic acid selected from the group consisting of SEQ ID NOs: 8-3795.

35. A method for identifying a gene which is required for proliferation of a cell comprising:

(a) contacting a cell with an antisense nucleic acid selected from the group consisting of a nucleic acid at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 8-3795 or a proliferation-inhibiting portion thereof, a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleic acid selected from the group consisting of SEQ ID NOs.: 8-3795 under stringent conditions, and a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleic acid selected from the group consisting of SEQ ID NOs.: 8-3795 under moderate conditions, wherein said cell is a cell other than the organism from which said nucleic acid was obtained;

(b) determining whether said nucleic acid inhibits proliferation of said cell; and

(c) identifying the gene in said cell which encodes the mRNA which is complementary to said antisense nucleic acid or a portion thereof.

36. A method for identifying a compound having the ability to inhibit proliferation of a cell comprising:

(a) identifying a homolog of a gene or gene product whose activity or level is inhibited by an antisense nucleic acid in a test cell, wherein said test cell is not the microorganism from which the antisense nucleic acid was obtained, wherein said antisense nucleic acid is selected from the group consisting of a nucleic acid having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a nucleotide sequence selected from the group consisting of SEQ ID NOs. 8-3795, a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleic acid selected from the group consisting of SEQ ID NOs.: 8-3795 under stringent conditions, and a nucleic acid comprising a nucleotide sequence which hybridizes to a

nucleic acid selected from the group consisting of SEQ ID NOs.: 8-3795 under moderate conditions;

(b) identifying an inhibitory nucleic acid sequence which inhibits the activity of said homolog in said test cell;

(c) contacting said test cell with a sublethal level of said inhibitory nucleic acid, thus sensitizing said cell;

(d) contacting the sensitized cell of step (c) with a compound; and

(e) determining the degree to which said compound inhibits proliferation of said sensitized cell relative to a cell which does not express said inhibitory nucleic acid.

37. A method of identifying a compound having the ability to inhibit proliferation comprising:

(a) sensitizing a test cell by contacting said test cell with a sublethal level of an antisense nucleic acid, wherein said antisense nucleic acid is selected from the group consisting of a nucleic acid having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a nucleotide sequence selected from the group consisting of SEQ ID NOs. 8-3795 or a portion thereof which inhibits the proliferation of the cell from which said nucleic acid was obtained, a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleic acid selected from the group consisting of SEQ ID NOs.: 8-3795 under stringent conditions, and a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleic acid selected from the group consisting of SEQ ID NOs.: 8-3795 under moderate conditions;

(b) contacting the sensitized test cell of step (a) with a compound; and

(c) determining the degree to which said compound inhibits proliferation of said sensitized test cell relative to a cell which does not contain said antisense nucleic acid.

38. A method for identifying a compound having activity against a biological pathway required for proliferation comprising:

(a) sensitizing a cell by providing a sublethal level of an antisense nucleic acid complementary to a nucleic acid encoding a gene product required for proliferation, wherein said gene product is selected from the group consisting

5-15
C1

5

10

20

25

30

of a gene product having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 8-3795, a gene product encoded by a nucleic acid having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a nucleic acid encoding a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 8-3795, a gene product having at least 25% amino acid identity as determined using FASTA version 3.0t78 with the default parameters to a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 8-3795, a gene product encoded by a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleic acid selected from the group consisting of SEQ ID NOs.: 8-3795 under stringent conditions, a gene product encoded by a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleic acid selected from the group consisting of SEQ ID NOs.: 8-3795 under moderate conditions, and a gene product whose activity may be complemented by the gene product whose activity is inhibited by a nucleic acid selected from the group consisting of SEQ ID NOs.: 8-3795;

- (b) contacting the sensitized cell with a compound; and
- (c) determining the extent to which said compound inhibits the growth of said sensitized cell relative to a cell which does not contain said antisense nucleic acid.

39. A method for identifying a compound having the ability to inhibit cellular proliferation comprising:

- (a) contacting a cell with an agent which reduces the activity or level of a gene product required for proliferation of said cell, wherein said gene product is selected from the group consisting of a gene product having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group

517
C1

5

10

15

20

25

30

consisting of SEQ ID NOs.: 8-3795, a gene product encoded by a nucleic acid having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a nucleic acid encoding a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 8-3795, a gene product having at least 25% amino acid identity as determined using FASTA version 3.0t78 with the default parameters to a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 8-3795, a gene product encoded by a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleic acid selected from the group consisting of SEQ ID NOs.: 8-3795 under stringent conditions, a gene product encoded by a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleic acid selected from the group consisting of SEQ ID NOs.: 8-3795 under moderate conditions, and a gene product whose activity may be complemented by the gene product whose activity is inhibited by a nucleic acid selected from the group consisting of SEQ ID NOs.: 8-3795;

(b) contacting said cell with a compound; and

(c) determining the degree to which said compound reduces proliferation of said contacted cell relative to a cell which was not contacted with said agent.

40. A method for identifying the biological pathway in which a proliferation-required gene product or a gene encoding a proliferation-required gene product lies comprising:

(a) providing a sublethal level of an antisense nucleic acid which inhibits the activity or reduces the level of said gene encoding a proliferation-required gene product or said said proliferation-required gene product in a test cell, wherein said proliferation-required gene product is selected from the group consisting of a gene product having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 8-3795, a gene product encoded by a nucleic acid having at least 70% nucleotide

5

10

15

20

25

30

511
C1

sequence identity as determined using BLASTN version 2.0 with the default parameters to a nucleic acid encoding a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs:8-3795, a gene product having at least 25% amino acid identity as determined using FASTA version 3.0t78 with the default parameters to a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 8-3795, a gene product encoded by a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleic acid selected from the group consisting of SEQ ID NOs.: 8-3795 under stringent conditions, a gene product encoded by a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleic acid selected from the group consisting of SEQ ID NOs.: 8-3795 under moderate conditions, and a gene product whose activity may be complemented by the gene product whose activity is inhibited by a nucleic acid selected from the group consisting of SEQ ID NOs: 8-3795;

(b) contacting said test cell with a compound known to inhibit growth or proliferation of a cell, wherein the biological pathway on which said compound acts is known; and

(c) determining the degree to which said compound inhibits proliferation of said test cell relative to a cell which does not contain said antisense nucleic acid.

41. A method for determining the biological pathway on which a test compound acts comprising:

(a) providing a sublethal level of an antisense nucleic acid complementary to a proliferation-required nucleic acid in a cell, thereby producing a sensitized cell, wherein said antisense nucleic acid is selected from the group consisting of a nucleic acid having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a nucleotide sequence selected from the group consisting of SEQ ID NOs:8-3795 or a proliferation-inhibiting portion thereof, a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleic acid selected from the group consisting of SEQ ID NOs.: 8-3795 under stringent conditions, and a nucleic

acid comprising a nucleotide sequence which hybridizes to a nucleic acid selected from the group consisting of SEQ ID NOs.: 8-3795 under moderate conditions and wherein the biological pathway in which said proliferation-required nucleic acid or a protein encoded by said proliferation-required polypeptide lies is known,

(b) contacting said cell with said test compound; and

(c) determining the degree to which said compound inhibits proliferation of said sensitized cell relative to a cell which does not contain said antisense nucleic acid.

42. A compound which inhibits proliferation by interacting with a gene encoding a gene product required for proliferation or with a gene product required for proliferation, wherein said gene product is selected from the group consisting of a gene product having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 8-3795, a gene product encoded by a nucleic acid having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a nucleic acid encoding a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 8-3795, a gene product having at least 25% amino acid identity as determined using FASTA version 3.0t78 with the default parameters to a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 8-3795, a gene product encoded by a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleic acid selected from the group consisting of SEQ ID NOs.: 8-3795 under stringent conditions, a gene product encoded by a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleic acid selected from the group consisting of SEQ ID NOs.: 8-3795 under moderate conditions, and a gene product whose activity may be complemented by the gene product whose activity is inhibited by a nucleic acid selected from the group consisting of SEQ ID NOs.: 8-3795.

43. A method for manufacturing an antibiotic comprising the steps of:

screening one or more candidate compounds to identify a compound that reduces the activity or level of a gene product required for proliferation wherein said gene product is selected from the group consisting of a gene product having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 8-3795, a gene product encoded by a nucleic acid having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a nucleic acid encoding a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 8-3795, a gene product having at least 25% amino acid identity as determined using FASTA version 3.0t78 with the default parameters to a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 8-3795, a gene product encoded by a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleic acid selected from the group consisting of SEQ ID NOs.: 8-3795 under stringent conditions, a gene product encoded by a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleic acid selected from the group consisting of SEQ ID NOs.: 8-3795 under moderate conditions, and a gene product whose activity may be complemented by the gene product whose activity is inhibited by a nucleic acid selected from the group consisting of SEQ ID NOs.: 8-3795 ; and manufacturing the compound so identified.

44. A method for inhibiting proliferation of a cell in a subject comprising administering an effective amount of a compound that reduces the activity or level of a gene product required for proliferation of said cell, wherein said gene product is selected from the group consisting of a gene product having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 8-3795, a gene product encoded by a nucleic acid having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a nucleic acid encoding a gene product whose expression is inhibited by an antisense

nucleic acid comprising a nucleotide sequence selected from the group consisting of
SEQ ID NOs:8-3795, a gene product having at least 25% amino acid identity as
determined using FASTA version 3.0t78 with the default parameters to a gene product
whose expression is inhibited by an antisense nucleic acid comprising a nucleotide
sequence selected from the group consisting of SEQ ID NOs.: 8-3795, a gene product
encoded by a nucleic acid comprising a nucleotide sequence which hybridizes to a
nucleic acid selected from the group consisting of SEQ ID NOs.: 8-3795 under stringent
conditions, a gene product encoded by a nucleic acid comprising a nucleotide sequence
which hybridizes to a nucleic acid selected from the group consisting of SEQ ID NOs.:
8-3795 under moderate conditions, and a gene product whose activity may be
complemented by the gene product whose activity is inhibited by a nucleic acid selected
from the group consisting of SEQ ID NOs: 8-3795.

5

10

SUB
C1

FILED "24251860

ADD
A3

ADD
B3